REMARKS/ARGUMENTS

By this Amendment, claims 1-2, 4 and 15-47 are canceled, claims 3, 5-10 and 14 are amended, and claims 48-61 are added. Claims 3, 5-14 and 48-61 are pending.

The Examiner's courtesy in granting a telephonic interview to the undersigned on November 1, 2007 is gratefully acknowledged. Applicant's separate record of the substance of the interview is incorporated into the following remarks.

Claim Rejection Under 35 U.S.C. § 112

Claims 1-14 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for isolated pluripotent adult stem cells from any species of vertebrate obtained from any exocrine gland tissue, wherein said pluripotent adult stem cells differentiate into any cell type. This rejection is respectfully traversed.

The foregoing amendments obviate this rejection by deleting claims 1-2 and incorporating the limitations of claim 4 into base claim 3.

During the interview, the undersigned pointed out that the nearly identical results with two divergent species of mammals (human and rat) show that the disclosure enables the full scope of the claims, which are now limited to the group consisting of specific exocrine glandular tissues from mammals. The Examiner acknowledged that the claims are enabled for rats and humans, but said that she might not allow claims to a genus based on working examples from less than three members of the genus. The Examiner acknowledged that rats and humans are two divergent species of the claimed genus, but suggested that Applicant provide evidence supporting enablement of a third species of the genus, so as to eliminate the possibility that the rat and human data are merely coincidental.

A Rule 132 Declaration providing evidence that the claimed invention is also enabled for a third species of mammal, namely goats, will be submitted in supplement to this Amendment.

Moreover, Dr. Kruse's previously submitted Rule 132 Declaration describes how experimental protocols described in the application were used to prepare isolated pluripotent adult stem (IPAS) cells from ***fourteen*** different species of animals.

With respect to the Examiner's argument that the marker "nestin" for cells from sudoriferous (sweat) glands is a specific neuronal stem cell marker and not indicative for an additional differentiation capability into muscle and exocrine cells, it should be noted that

according to more recent literature, nestin is currently considered as a general stem cell marker. See, e.g., Wiese et al., "Nestin expression--a property of multi-lineage progenitor cells?" Cell Mol Life Sci. 2004 Oct;61(19-20):2510-22 (submitted herewith) and Zulewski et al., "Multipotential nestin-positive stem cells isolated from adult pancreatic islets differentiate ex vivo into pancreatic endocrine, exocrine, and hepatic phenotypes." Diabetes. 2001 Mar;50(3):521-33 (previously of record). In particular, see the abstract of Wiese et al., which states

> We show that nestin is abundant in ES-derived progenitor cells that have the potential to develop in neuroectodermal, endodermal and mesodermal lineages.

Thus, currently prevailing knowledge in the art supports Dr. Kruse's assertion that he has been able to use the teachings of the original disclosure to prepare IPAS cells from fourteen different species of animals, including many different types of mammals.

Accordingly, reconsideration and withdrawal of the enablement rejection are respectfully requested.

Claim rejections under 35 U.S.C. § 102

Claims 1-14 stand rejected as allegedly being anticipated under 35 U.S.C. § 102(b) by Schneider et al. as evidenced by Kruse et al., and by Apte et al. as evidenced by Kruse et al. These rejections are respectfully traversed.

As discussed during the interview, isolated stem cell claims 3 and 5-9 are amended to composition claims to clarify that only the specified cells are being claimed. Base composition claim 3 employs the transitional phrase "consisting of", thus excluding from the composition differentiated cells such as those included in the compositions disclosed by Schneider et al. and Apte et al.

Both Schneider et al. and Apte et al. disclose the isolation and cultivation of cells which are described as a kind of differentiated cells, namely myofibroblast-like cells according to Schneider. In contrast to the method used in the present invention, the protocols for cultivating and propagating do not recite a step of separating differentiated cells from undifferentiated stem cells to obtain pure stem cell cultures. (With the exception of the first passage wherein contaminating acinar cells, ductal cells, fibroblast and endothelial cells are removed. In this case, however, the differentiated cells are remnants of the original tissue and not later grown

differentiated cells.) On page C540, Schneider et al. explicitly states that almost 100 % of the PSC in late primary culture and subsequent passages were SMA positive. SMA ("smooth muscle actin") is widely recognized as a marker for muscle cells (compare also the corresponding cell-characterizing experiments in the present application) and used by Schneider to identify their cells as "myofibroblast-like cells".

As acknowledged by the Examiner during the interview, these myofibroblast-like cells are excluded from the composition of claims 3, 5-9 and 59-61 by the transitional phrase "consisting of". Thus, these claims are not anticipated by the cited art.

Claims 10-13 are directed to a stem cell culture consisting essentially of the composition of claim 3 and a culture medium adapted to allow stable maintenance and proliferation of the cells essentially without differentiation.

The adult stem cells of the stable long-term cultures disclosed in the present application show no or only a very low differentiation activity in adhesion culture (and a low percentage of SMA-positive cells; unpublished results) and only after induction by cultivation in hanging drops and forming of organoid bodies, a significant differentiation can be observed. Thus, even if the cell cultures of Apte et al or Schneider et al., respectively, may have actually contained some adult stem cells, those mixed cell cultures certainly cannot be considered as equivalent to the essentially pure and long-term stable cell cultures disclosed in the present invention.

Thus, the "consisting essentially of" transitional phrase excludes from these claims the differentiated cells of Schneider et al. and Apte et al, which would have a material impact on the claimed culture. Accordingly, claims 10-13 are not anticipated by the cited art.

Claim 14 is directed to a primary stem cell culture wherein a majority of living cells present in the culture are undifferentiated pluripotent adult stem cells and the primary stem cell culture is obtained from exocrine glandular tissue from a salivary gland, a lacrimal gland, a sudoriferous gland and/or a sebaceous gland of a mammal. Apte et al. and Schneider et al. teach only the use of pancreatic tissue, and do not therefore anticipate claim 14.

Accordingly, reconsideration and withdrawal of the anticipation rejections of claims 1-14 are respectfully requested.

New Claims

New claims 48-50 specify that the cells are derived from exocrine glandular tissue of a salivary gland, a lacrimal gland, a sudoriferous gland, and/or a sebaceous gland. As noted above, Apte et al. and Schneider et al. teach only the use of pancreatic tissue. Thus, these claims are not anticipated by the cited art.

New claims 51-58 are directed to a primary stem cell culture wherein living cells present in the culture consist essentially of (or consist of, in the case of claim 52) undifferentiated pluripotent adult stem cells. Again, these transitional phrases exclude from the claimed culture the differentiated cells of Schneider et al. and Apte et al. Thus, these claims are not anticipated by the cited art.

New claims 56-61 are species-specific claims added to more completely claim the full scope of the invention. These claims, which find support in the specification at, e.g., page 3, lines 27-30, are not anticipated for at least the same reasons as the claims from which they depend.

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicant's undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

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By_____

David M. Tener
Registration No. 37,054
Customer No. 03000
(215) 567-2010
Attorneys for Applicant

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